Abstract

Background and Objective: Telomerase is in charge of telomere extending. It is triggered in about 90% of cancer cells. hTERT is the controlling subunit of telomerase and plays a critical role in the activation of telomerase. The mechanism through which hTERT regulate the invasion and metastasis of cancer is unclear. miRNAs are the novel regulator of gene silencing and can target hTERT by binding the 3' UTR of its mRNA, and regulate gene expression. In the previous study reported that miR-1266 can target hTERT in gastric (SGC-7901) cancer. In this study, we have made the first report of miR-1266-5p role on the hTERT expression, its various transcripts, telomerase activity, and biological functions, including cell proliferation and cell cycle in AGS, MCF7, A375, and HepG2 cells.

Methods: For investigating the function of miR-1266-5p, we used chemically synthesized oligonucleotide mimics and inhibitors. AGS, MCF7, A375, and HepG2 cells were transfected with miR-1266-5p mimic, inhibitor, and just HiperFect reagent as a negative control. The Expression levels of miR-1266-5p, hTERT, its variant transcripts, and transfection efficiency were analyzed by Taqman qRT-PCR. The cell proliferation and cell cycle changes were detected by MTT calorimetric assay and flow cytometry, respectively. Also, Quantitative TRAP Assay was used to detect telomerase activity.

Results: The results showed that the expression of miR-1266-5p significantly was increased after transfection by mimic compared to control cells, while its expression was decreased in transfected cells by the inhibitor. Also, we confirmed that upregulated miR-1266-5p significantly decreased cell growth, although inhibitor promoted cell proliferation. This finding was confirmed by cell cycle analysis, as upregulation of miR-1266-5p induced cells cycle arrest at the transition of G1 to S phase and led to G0/G1 entry, while the downregulation of miR-1266-5p promoted cell growth and led to G2/M entry. Concordantly, the overexpression of miR-1266-5p resulted in down-regulated hTERT expression and also suppressed telomerase activity. Also, upregulation of miR-1266-5p decreased full-length variant and increased alpha variant compared to transfected cells by inhibitor and control cells.

Conclusion: our results demonstrated that miR-1266-5p can target hTERT expression and telomerase activity in the Gastric (AGS), Breast (MCF7), Liver (HepG2), and Melanoma (A375)

cancer cell lines, so acts as hTERT and telomerase activity suppressor. miR-1266-5p could also decrease cell proliferation and induce cell cycle arrest, while its inhibition eliminates miR-1266-5p effects. In addition, miR-1266-5p can affect hTERT variants in AGS cell line and alter their expression as well as result in downregulate of hTERT expression. Thus, upregulation of miR-1266-5p may be a serve as a novel therapeutic target in AGS, MCF7, A375, HepG2 cell lines. Thus, delivery of miR-1266-5p to these cells can be an effective therapeutic target for the treatment of Gastric, Breast, Liver, and Melanoma cancers.

Keywords: miR-1266-5p, hTERT, telomerase activity, cancer cell lines